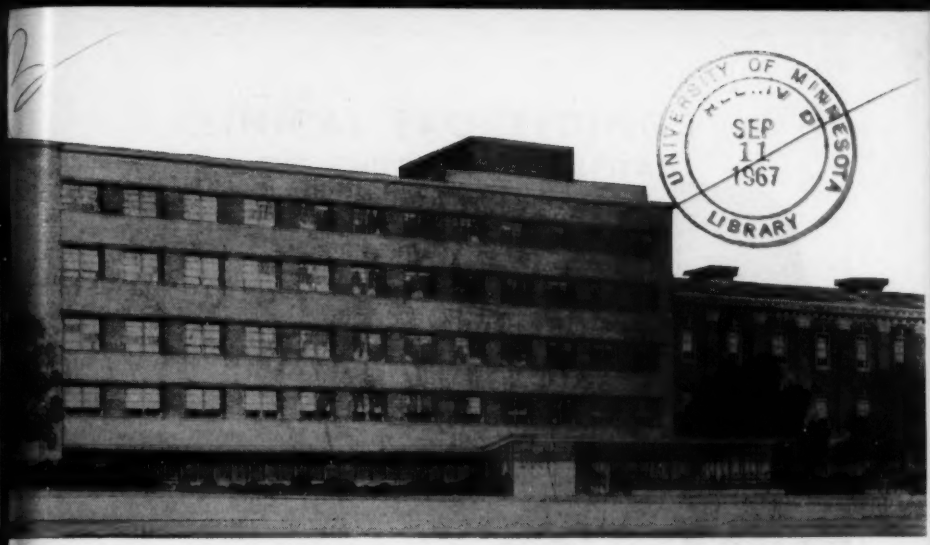

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VOLUME XIII December 1957 NUMBER 12

Clinical Proceedings

OF THE CHILDREN'S HOSPITAL

WASHINGTON, D. C.

RADIATION HAZARDS IN CLINICAL MEDICINE. *Benedict J. Duffy, Jr., M.D., Robert L. Brent, M.D., Robert W. Miller, M.D., William Moloney, M.D., Robert J. Nelsen, D.D.S.* 247

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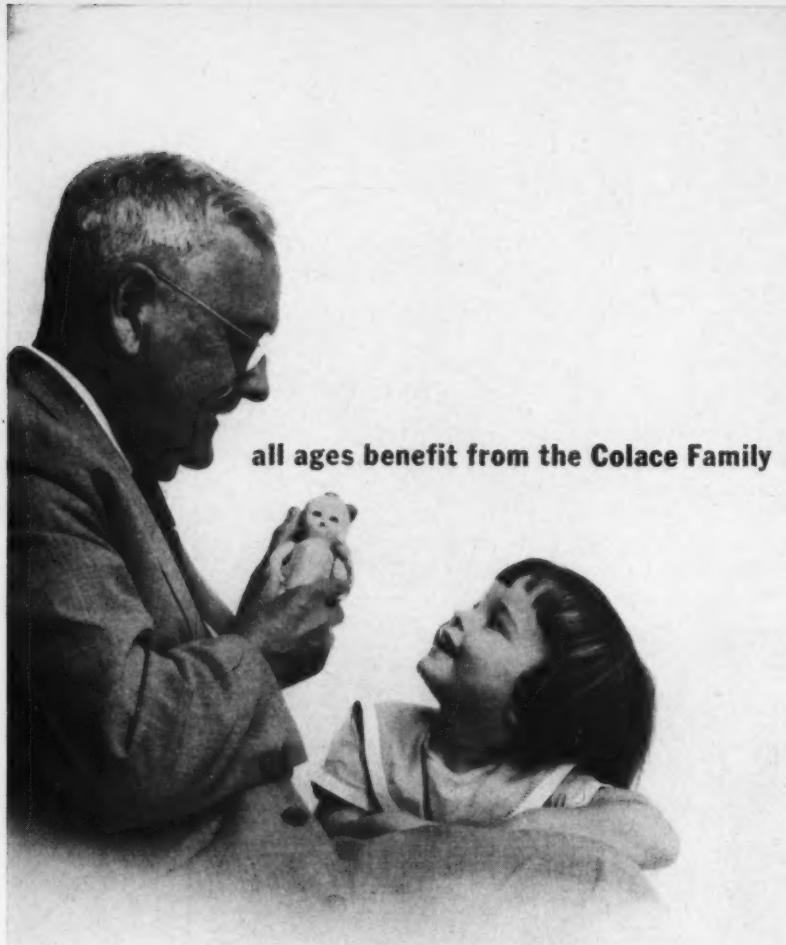

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PUBLISHED MONTHLY BY THE STAFF AND RESEARCH FOUNDATION OF THE CHILDREN'S HOSPITAL, WASHINGTON, D. C.

Cases are selected from the weekly conferences held each Friday at 12:30 P.M., from the Clinicopathological conferences and from the monthly Staff meeting.

This bulletin is printed for the benefit of the present and former members of the Attending and Resident Staffs, and the clinical clerks of Georgetown and George Washington Universities.

Subscription rate is $3.00 per year. Those interested make checks payable to "Clinical Proceedings Dept.," The Children's Hospital, Washington, D.C. Please notify on change of address.

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Entered as second class matter November 21, 1946 at the post office at Washington, D.C., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 538, Act of February 28, 1925, authorized January 17, 1947.

RADIATION HAZARDS IN CLINICAL MEDICINE

Panel Symposium

Benedict J. Duffy, Jr., M.D.,* Robert L. Brent, M.D.,† Robert W. Miller, M.D.,‡ William Moloney, M.D.,§ Robert J. Nelsen, D.D.S.‖

Dr. Duffy:

One of the interesting by-products of the atomic age has been an increased public interest and awareness of the hazards of radiation. A recent example occurred in a national lady's magazine which had a rather frightening banner across the front of it saying "Is radiation killing our children?". One of the purposes of this discussion is to present some answers to this question. *Is* radiation in any way reducing the longevity of any of our children? With regard to the adult group, Dr. Shields Warren has recently presented a study of the effect of radiation on physicians. This study seemed to prove that physicians who used radiology in their practice lived an average of 5.2 years less than the non-radiologists. They died of the usual diseases, but they died sooner. The implication was very strong that radiation was the cause of their earlier demise. Again, is this a fact?

Any discussion of radiation must rely on a certain amount of experimental data, but the panelists have been asked to restrict themselves, wherever possible, to the practical clinical problems that relate to radiation exposure. The following axioms are well accepted I think, by the entire panel. The first is that radiation in skillful hands, judiciously used, has saved lives and is a very valuable clinical adjunct to our treatment of disease. Secondly, there are no absolute facts regarding the mechanism of radiation damage. Finally, all of us realize that an agent so subtle and powerful as radiation would have to have the potential of acting against other than abnormal cells.

With these few postulates in mind, I would like now to present Doctor Robert Brent, Chief of the Radiobiology Division of the Walter Reed Army Research Institute who will discuss the nature of radiation effects.

Sponsored by Medical and Dental School, Georgetown University and the Medical Education for National Defense Program.

* Assistant Professor of Medicine, Georgetown University Medical Center.

† Chief, Radiobiology Division, Walter Reed Army Research Institute.

‡ Professional Associate, National Academy of Sciences.

§ Associate Professor of Medicine, Tufts University School of Medicine.

‖ Clinical Assistant Professor of Dentistry, Georgetown University Medical Center.

Dr. Brent:

I wish first to discuss the primary effect of radiation in the tissues in order that you may have some understanding of what radiation may do to the body in the first instant, in the first few minutes, and in the first few days. Next I will attempt to analyze two fields, radiation genetics, and radiation embryology, in an effort to determine where experimental data can and cannot be adapted to the human problem.

Any evaluation of radiation and its biologic effect must of necessity start with many definitions. I think that we are all familiar with the term "roentgen", but I would like to point out some of the misconceptions about what the term "roentgen" means and how it differs from some of our other medical measurements. First of all the roentgen differs from the dosage used in administration of drugs or medicine, in the sense that the roentgen is a dose *delivered* to the tissue; it is the dose which actually gets to the tissue. A roentgen was originally defined as being equivalent to a certain amount of charge which is dissipated in the tissue. Again, keep in mind that it is the tissue's response to the radiation. The dose is only indirectly related to the radioactive or emitting source so far as the measurement of the radiation received is concerned. Thus it is erroneous to discuss how many roentgens an x-ray machine is delivering unless one knows the distance and position of the patient.

Another definition of the roentgen has to do with the number of ion pairs that are produced in the tissue. In general the roentgen can be defined in any term which represents tissues affected and energy dissipated in the tissues. It does not make any difference whether it is defined in terms of ions produced, of a charge produced, of calories dissipated in tissues, of electron volts, or of ergs; all can be part of the definition of a roentgen.

How does all this energy dissipated in tissue produce a lethal reaction? Take for example a dose of 1000 roentgens or "r", which by all our standards would produce 100 per cent mortality in the human subject. This would be equivalent to 10^{15} ionizations. In other words in each cubic centimeter of tissue, 10^{15} free radicals would be produced throughout the body. An individual liver cell has an average volume of 12 cubic microns which is equivalent to a volume of 12×10^{-9} cubic centimeters. 10^{15} ionizations per cubic centimeter would deliver two million ionizations to each liver cell. If we estimate that there are 2×10^{9} protein molecules in each cell, for every thousand molecules in the liver cell one will be ionized or will have an ionization produced in its molecular structure. Here is a process which is affecting only one in a thousand molecules within each cell in the body, and yet it is able to cause death in a particular organism. This seems in-

credible, and I think that we might offer to postulate the mechanisms involved.

The first hypothesis put forth was that radiation produced toxic breakdown products, and these toxic breakdown products caused death. The second was that in each cell there are only a few enzymes and that the destruction of these particular enzymes by ionization produced death. The last postulate was that ionization could possibly evoke a chain chemical reaction which would not subside until the original ions united and neutralized each other. I think the point is that we really do not know which of these, if any, is responsible for the so-called primary cause of radiation death.

Our knowledge of radiation death can be broken down into three categories. The first is the so-called *primary ionization* about which we know a great deal. We know a number of the radicals produced, and we know something of the length of time that ionizations last. We are also quite familiar with the effects of the second step, the *chemical changes*. We know about the changes in blood sugar, the changes in the nucleic acid and the changes in enzyme content of tissue. We know a great deal about the chemical changes from radiation, but of the instantaneous step, between ionization and these chemical changes, we are very ignorant. The third stage of successive biologic changes we know a great deal about. This is practically 90 per cent of our knowledge of radiation damage: the *hematological damage*, the blood coagulation defects, the skin telangiectasias, the nausea, vomiting, and the central nervous system effects. We are quite familiar with all these so-called biological effects of radiation. The big defect in our knowledge at the present time is the mechanism by which step 1 (primary ionization) causes step 2 (chemical changes). Although only one in one thousand molecules is affected in an animal which receives total body radiation, every single cell in the body is going to have some ionization. When compared with any other injury the body may receive, as for instance, a severe burn, a crushing injury or a toxic chemical which destroys a large segment of the kidney, radiation affects every tissue and every cell in the body. This is the one big difference of radiation from all other injuries that the body receives. The second big difference between radiation injury and other injuries is the extent of our ignorance of the mechanisms, namely, the step between the primary ionization and the chemical changes. We are not even sure whether this is a physical event or a chemical event, or whether it is due to a focal rise in temperature due to the energy which is dissipated in the tissues. I hope this short discussion gives you some idea of our lack of knowledge of radiation damage, and more important, our real lack of understanding of why we do have death when we are doing such a minute amount of injury to the protein structure of the body.

The two particular fields which I would like to discuss with respect to their adaptation to the human problem are radiation genetics and radiation embryology. It is in these fields that we know the least and therefore axiomatically worry the most. I would like to discuss them from the standpoint of how much experimental data in animals can be applied with reasonable assurance to human problems.

The sensitivity of the embryo to noxious agents has been known for years. The fact that the embryo is more sensitive to radiation than the adult came as no surprise to the experimental embryologist. Let us look at some of the findings of which we are now aware with respect to the sensitivity of the embryo and the sensitivity periods in the embryo.

The rat has a gestational period of about 21 or 22 days, and congenital malformations in the rat are most easily produced on the ninth or tenth day of gestation. Congenital malformations of the central nervous system can be produced throughout organogenesis; on the other hand, other organ systems, the genito-urinary system, the cardiovascular system, and the face, have more definite peaks of sensitivity and much shorter periods during gestation in which congenital malformations can be produced by radiation. These facts are somewhat disturbing and rightly so. If the rats' gestational period is 22 days and the sensitivity period makes up 6 or 7 days of that period, there is at least 30 per cent of the gestation period of the rat during which most of the organs of the body are highly susceptible to radiation. Does this mean that man has a very sensitive period to radiation during 30 per cent of his gestational period, and that congenital malformations may be produced by radiation during the entire first trimester of pregnancy, for instance? Application of such experimental data in the rat to human beings can be erroneous.

How sensitive are human embryos to radiation compared to the adult human? On the eight and ninth days of gestation in the rat, 200 roentgens will kill all embryos. It is not until the eleventh and twelfth days of gestation, when the organs are beginning to develop, that embryos require more than 200 roentgens to destroy them in entirety. In the adult human the LD50 may be 450 to 600 roentgens, or the dose necessary to kill all exposed adults may be as high as 700 or 800 roentgens. The embryo then is far more sensitive to radiation.

How much of the human gestational period, compared to the 30 per cent of the rat, is the sensitive period? The rat's first third of gestation is almost exactly the same as the human. We realize that the human embryo implants approximately at the eight or ninth day, and the rat embryo implants at the seventh day. In other words, implantation occurs only a day or a day and a half later in the human. On the other hand, the next five days of the rat's gestation are its most sensitive period to radiation.

This period corresponds to the second week to the sixth week in the human. In other words, less than 10 per cent of the human embryonic period has a so-called *highly* susceptible period instead of 30 to 35 per cent as in the rat. This fact would explain the infrequency of congenital malformations in human embryos following irradiation as compared to the rat. Furthermore, since the central nervous system remains sensitive for a relatively longer time it would explain the high incidence of microcephaly and mental retardation in human embryos which were irradiated.

Next, the problem of radiation genetics. This subject has the most conflicting views of all, mainly because proving or disproving the presence and the extent of genetic changes in humans is a very long term project, and at the present time we have not observed the individuals in Hiroshima or Nagasaki for a long enough period. Since Muller's Nobel Prize winning paper in 1927, literally thousands of experiments have been done to determine mutation rates on every type of living organisms from plants and lower animals all the way up to mammals.

First, what is meant by the mutation rate? The first concept to keep in mind is that the mutation rate never applies to an entire organism unless one is referring to average mutation rates. Mutation rate specifically applies to one individual trait, one individual locus on a chromosome. If it is desired to define the mutation rate of a particular genetic trait, it might be said to be the probability of occurrence or the rate of occurrence of a genetic alteration in the total population of ovocytes and spermatocytes. It is a probability that an abnormal genetic constitution will occur in a previously normal population. These mutation rates have been calculated for traits in living organisms ranging from maize, bacteria, and Drosophila, all the way to mammals including humans. The problem today is to determine how much of these accumulated data can be applied to humans. There is no doubt in anyone's mind that mutations are produced in mammals by irradiation. The original skeptics who claim that no understanding of mammalian genetics could be derived from studying Drosophila have quietly passed out of the picture. Dominant lethals, sublethals, subvitals, dominant visibles, recessive lethals, and on and on—every possible type of mutation which can occur and has been observed in the Drosophila has been observed in rodents, mice, and rats. The *average* mutation rate is ten times as great in mammalian organisms as it is in Drosophila. For example, one way of talking about a mutation rate is the probability of one roentgen producing a mutation at a specific locus on a gene. In Drosophila this approximates 10^{-8}, or one in a hundred million. On the other hand, in mammals the *average* of the traits studied is around 10^{-7}, or one in ten million. Of course, there are many more genes in mammals than there are in the Drosophila, because of the higher number of chromosomes. There-

fore, for two reasons the genetic problem would seem to be more important and more severe in mammals and humans than in Drosophila. First, the mutation rate is higher spontaneously, and occurs more readily with irradiation, and second, there are more genes to be affected.

What factors may lessen the genetic response of mammals to stimuli causing mutations? First of all, we have studied only a few mutations in mammals, only several score in rodents, for example. These are very likely to be the very easily mutatable gene sites, and of the chromosomes in the human, and the thousands and thousands of genes that lie in these chromosomes, there may be very low spontaneous mutation rates. In other words, their chance of mutating is very small, and therefore, there may be little chance of being affected by radiation. Secondly, most experiments are carried out under optimal conditions for producing mutations, such as radiating an organism each day, or radiating an organism once a week and mating them during that time. Experiments have shown that the longer the wait after exposure to radiation the less the number of mutations that are found in the sperm or ova, until a plateau of permanent mutations for that organism is reached. Here then, are two factors which may decrease the genetic effects in the human population.

According to genetic theory most of the mutations produced by irradiation are recessive and therefore would not appear in the first generation, but we have to look for the dominant lethals and translocations in the first generation. There are a number of mutations that could occur in the general population which could not possibly be picked up because of their nature. One of them is the typical translocation which produces semi-sterility. In this condition, part of the chromosome is dissociated by the radiation, and reassociates with another chromosome, so that one chromosome ends up with an excess of genes and another chromosome with a deficiency of genes. The genetic resultant is that every other pregnancy, statistically, will end in death very early in gestation, so early that in the human, abortion would not even be recognized. This has been very well documented in mammals, and the complete story of the type of congenital malformation, the type of death, and particularly the time of death (the first four weeks) in the human, means that semi-sterility could be present in the population at the present time, and could not possibly be discovered by our present medical records.

What about the possibility that all mutations that are present in the population are due to radiation? Wright postulates that only three roentgens applied to the entire body is necessary to double the average mutation rate, but there can be a sizable error in talking about an average mutation rate because the few mutations that we know about may not be anywhere near the average mutation rate for all the genes on the 46 chromosomes.

Wright's postulate of three roentgens to double the mutation rate is approximately the same as the background radiation that an individual receives in his first generation of life. Therefore, according to Wright, all mutations can be accounted for by background radiation. This is the same theory that Haldane put forth. Muller's estimate of 25 roentgens to double the mutation rate would not explain all mutations on the basis of background radiation alone. Russell, on the other hand, calculates that three hundred roentgens are necessary to double the mutation rate.

There are a number of problems that we cannot resolve at the present time, and I think that before we can definitely say whether the Drosophila is more or less sensitive to radiation than the human we are going to have to know a great deal more about the other genes on the chromosomes in the human.

Dr. Miller:

The only way that a relationship of radiation to any disease can be demonstrated is through a difference in the incidence when heavily irradiated and non-irradiated populations are compared. Dr. Brent has already mentioned the animal experimentation with regard to embryologic effects. In 1935 in this country an obstetrician in Philadelphia showed that pregnant women treated in the first trimester of pregnancy with radiation for pelvic disease gave birth to abnormal children, principally children with microcephaly and mental retardation. This finding has been confirmed among children who were exposed *in utero* to the atomic bombs in Hiroshima and Nagasaki.

The incidence of these cases increases as the distance from the hypocenter, the center directly under the bomb, decreases. This is particularly true in the group whose mothers had last menstruated seven to fifteen weeks prior to the bomb explosion. In this group there were 8 children whose mothers were within 1200 meters of the hypocenter, and all 8 of them had microcephaly and mental retardation. As the distance from the hypocenter increased, the numbers of these patients decreased and in their place occurred individuals whose head circumferences were smaller than usual but whose intelligence was normal. This is, in a sense, a transitional group between those who had a central nervous system defect that caused them to be mentally retarded, and those who were completely normal. There was a slight spill-over of abnormal cases into the neighboring gestational age groups, but for the most part the abnormalities occurred in children whose mothers had last menstruated seven to fifteen weeks before the bomb.

There were 15 children who had a combination of defects, and in 13 of these the mothers had lost some of their hair as a result of the radiation

exposure. This would indicate to a radiologist that the dose of radiation was rather high. Radiologists suggest that it might be over 200 roentgens. It is complicated to estimate though, because the mother's pelvis might have shielded the child from some of the radiation.

At any rate, the bulk of the cases occurred within 1800 meters of the hypocenter. Some of the patients had associated defects; three had strabismus, three had congenital dislocation of the hip, and two had mongolism. On the basis of the small number of total cases we do not know whether these are radiation effects or not. Other *in utero* effects occurred. One of the patients was of normal intelligence but had congenital dwarfism, strabismus, and nephritis. One of the patients with microcephaly died at the age of seven years with a primary carcinoma of the liver. This again does not mean that carcinoma of the liver is a late effect.

There is one other possible *in utero* effect that is not indicated by the Atomic Bomb Casualty Commission studies. Although there have been no cases of leukemia to date in our small group, in England a recent study of the histories of children who developed leukemia before they reached the age of 10 years showed a possible *in utero* effect of radiation exposure. In a pilot study Dr. Stewart analyzed the histories of 269 children who had leukemia, and found that in 43 cases diagnostic films of the mother's abdomen had been taken during pregnancy. An additional 269 children who did *not* have leukemia were matched with regard to age, sex, and locality with these patients, and only 24 of their mothers had received diagnostic radiation to the abdomen during pregnancy. Dr. Stewart and her associates call attention to this fact, not to indicate that radiation to a pregnant mother is contributory to leukemia, but to call attention to the fact that it might be. She is doing further studies to try to determine whether or not this is true.

From the Atomic Bomb Casualty Commission work one may feel that there was a reasonably large margin of safety in producing embryologic injury. From Dr. Stewart's studies one would think that a longer observation period might indicate that even small doses of radiation could be detrimental to the fetus.

Dr. Brent has pointed out that other effects occur in animals exposed to radiation as embryos, but this does not occur in the human, at least as far as we now know.

The annual incidence of leukemia in Japan in the group who were resident in Hiroshima at the time of the bomb explosion who were within a thousand meters of the hypocenter, and who had epilation or purpura as an acute radiation effect, was 240 cases per 100,000 population per year, an incidence 80 times normal. The incidence drops rapidly and reaches almost normal levels at a distance of 1500 meters from the hypocenter. For all practical

purposes it would seem reasonable to state, then, that the cases of leukemia within 1500 meters of the hypocenter are radiation-induced. This increased incidence of leukemia, incidentally, occurs at all ages.

Radiation cataracts have received a great deal of publicity because physicists in this country who were exposed to cyclotrons have developed radiation cataracts of a severe degree. I believe there are 14 such physicists. In Japan a search was made for these lesions. In 1949 it was found that there were 9 patients in Hiroshima with severe cataracts which could be reasonably attributed to their radiation exposure. These patients developed their cataracts between 6 months and 2½ years after their exposure. There was only one patient in Nagasaki. No more cases seem to be developing. The grade 3 and 4 cataracts that were radiation induced have in no instance caused the patient's vision to be worse than 20/70.

Polychromatic granular plaques on the posterior capsule of the lens are 8½ times more common in the patients heavily exposed to radiation. This lesion does not indispose the patient at all; he does not know it is present.

There has been an extensive genetic study in Japan. Eighty thousand babies were studied to determine whether or not genetic mutations could be detected in the first generation. A 241 page report of this work has just been published by the Academy of Sciences, and in summary, it states that, "while the authors have no doubt that genetic effects occur, as based on theory drawn from experiments on mice, fruit flies, and lower organisms, under the circumstances of our study no genetic effects could be found. If genetic effects did occur they were not great enough to cause the malformation rate to double".

One of the more recently defined possible late effects suggested by laboratory experimentation is premature aging. Affected animals become gray early; they lose their vigor; and they die in middle age of the diseases that usually occur in old age. In the human being this could be detected by a comparison of the mortality rates, and such a study is being undertaken in Japan, but no results are yet available.

A group in Rochester, N. Y. studied 1400 children who were given radiation to the thymus gland in childhood up to 25 years ago. They found an increased incidence of leukemia and an increased incidence of cancer of the thyroid in these children. The suspicion is that the radiation caused these two diseases to occur. It has not been shown yet, however, that the enlarged thymus itself did not predispose the child to these diseases. In other words, controls, individuals with large thymuses who had not received radiation, were not available.

What does this all mean in the practice of medicine? First of all, the effects in Hiroshima are the results of whole body irradiation. In the clinical practice of medicine, obviously, only parts of the body are irradiated.

The most critical organs are the gonads, because that is where the genetic mutations occur, and this is only of consequence in people who are still in childbearing age. The problem is of primary importance to the physicians and dentists responsible for the care of individuals who have not yet completed their families. The Academy of Sciences and the British Medical Research Council both indicate that for the population at large the dose to the gonads between conception and the age of 30 years should not exceed 10 roentgens. For the individual, 50 roentgens before the age of 30 was recommended as the maximal allowable dose. The British then went on to advise that not more than one in 50 individuals should receive that dose. The British also stated that for the somatic effects, the leukemia in particular, up to 200 roentgens of whole body radiation was safe. This latter figure is in doubt, however.

What are the radiation dosages incurred during the various diagnostic x-ray procedures? An intravenous pyelogram in the male delivers 6 to 7 roentgens. The female's soft tissues and abdominal muscles shield the ovaries so that they receive only a sixth of the male dose. For fluoroscopy the output depends in part on the efficiency of the machine. In a well run hospital a fluoroscope may put out as little as 1.5 roentgen per minute, but the mode for machines used throughout the country is 10 to 20 roentgens per minute. This is not so important genetically unless the gonads are in the field of radiation. However, in pediatrics it is a common practice in certain parts of the country for pediatricians to do a monthly fluoroscopic examination throughout the first year of life to impress the mother with the thoroughness of the examination; the gonads may be in the field of radiation during this needless procedure. Poor machines may put out as many as 120 roentgens per minute.

When the x-ray produces its biochemical effect by ionizing the cell, the cell re-arranges itself in a stable form. If this stable form is not toxic and does not cause the cell to malfunction, no damage is done. Most somatic cell changes are apparently reversible. However, it is felt that a small number of changes are irreversible. Certain strategic material injured by radiation may not revert to normal. This is particularly true in the case of genetic material. It is possible for this to occur in any cell in the body, and in theory, at least, the cell could lie dormant for a long period of time before finally becoming malignant or undergoing degeneration. It is possible as the patient passes through the stresses of life, infections, aging, adolescence, for example, that this leads one step closer to clinical disease.

This does not mean that x-rays should be abandoned. It simply suggests that radiologic procedures be limited to matters of medical necessity. When x-ray examination is important to the diagnosis, it should be done in the manner that will give a satisfactory diagnosis and lead the patient

to satisfactory treatment. It does seem reasonable to eliminate all elective x-rays that really do not contribute to the welfare of the patient, such as prophylactic irradiation of thymus glands or screening individuals by fluoroscopy when they could be screened by film studies equally well.

Dr. Duffy:

We are reasonably safe in using radio-isotopes for diagnosis because the type of isotope we use is selectively localized within a given area, and has a short half life which we can measure. Most of the radio-isotopes in common use are predominantly beta ray emitters, and the range of penetration of these rays is relatively little. We do not use tracer doses in pregnant women and lately we have been restricting their use to a great degree in children. We have reason to believe that the adult with otherwise normal body function is not as susceptible as is the child to small amounts of radiation. We do not think that careful study of the thyroid gland with I^{131} adds significantly to the total body radiation burden. Since we are treating patients with cancer when we give therapeutic doses of radiocolloids, I need not discuss that further. The condition warrants the treatment.

We have recently re-emphasized the hazards of medical fluoroscopy at Georgetown University Medical Center. We have made an effort to orient all our medical students and house staff toward the proper operation of the medical fluoroscopy machines. We encourge them to wear protective devices, to allow their eyes to adapt before turning on the machine, and to fluoroscope for only a minimal amount of time so as not to overexpose either themselves or the patient. It is possible in a teaching hospital for a patient to be subjected to repetitive fluoroscopy to amounts of as much as 1200 to 1400 roentgens by successive groups of physicians making sure that everybody gets a good chance to look at whatever interesting anomaly this patient might have.

Whatever is necessary for the proper care of that patient should be done but it must be constantly evaluated against the hazards of repeated diagnostic fluoroscopic procedures. We must be careful that we are no longer indulging a diagnosis but are actually giving therapeutic amounts of radiation.

Dr. Moloney:

Recently, at the Boston City Hospital, influenced by my experience with the Japanese, we attempted to adapt some of this knowledge to clinical problems. We discovered several interesting things. In the first 117 replies from 700 children who had received an average of 135 roentgens to the area of the thymus gland up to 25 years previously we have had one patient with cancer of the thyroid and four others whom we strongly

suspect have some form of tumor in and around the neck. This may not be statistically significant, but it is very interesting. We have not yet seen any leukemia. I would like to point out that all analyses of radiation effects in the human are based strictly on statistics.

Dr. Damashek said recently at a meeting in Boston that he was personally impressed with the possibilities of a leukemogenesis arising from medical radiation. He brought out some startling points. One was that in a full mouth x-ray one gets about 300 roentgens. I do not know this to be true, but if this is so, it is certainly interesting. One of the points that I would like to make is the possibility that the leukemogenic effect of radiation is not that of whole body radiation necessarily, but that there may be a target effect or an end organ effect.

I think it is perfectly true that one of the few statistically proven points is that leukemia in man can be caused by radiation. For 45 years we have been getting sporadic reports of leukemia in physicians who are exposed to radiation although the increased use among radiologists of x-ray protective devices should decrease the incidence of leukemia among this group. I have distinct reservations about the manner in which some of the data on clinical radiation leukemia have been acquired. For instance, March's figures are based on only 29 cases of leukemia taken from the obituaries of the American Medical Association. We are not at all sure that their diagnoses would be correct; the dose of radiation was unknown, and the duration of radiation in large part was also unknown. It should be pointed out that when a statistical method is used the interpretation is no better than the data to which the statistical method is applied even though the method be very good. Any data collected in the future should have a very strong component of high radiation dosage, and secondly, very accurate hematologic data.

We investigated all the people who were under 2000 meters from the hypocenter at Hiroshima, and studied all the cases of leukemia that occurred in that population over a period of years up until January 5, 1954. In comparing the group that was within the 2000 meter range who had evidence of heavy radiation by history (epilation, purpura), with another group, lightly radiated, we found 14 cases of leukemia. I do not think that anybody can quarrel that there is statistically very valid evidence of the leukemogenic effect of radiation and a dose-effect relationship.

In the last 5 months in the Boston City Hospital, I have seen three cases of acute leukemia in the adult, appearing in people who had extensive radiation. The first was a man with a seminoma who had received 7000 roentgens from a 2 million volt machine. The second was a woman who had innumerable x-rays including 5 or 6 gastrointestinal series with fluoroscopy, radiation treatment following mastectomy, and radiation to her

shoulder for bursitis. Within 5 years this woman had acute leukemia. The third was a woman with extensive radiation of the pelvis who some years later appeared at the hospital with acute leukemia. These cases are certainly not statistically significant but again are very interesting.

The British have been investigating the effect of a rather large dose of radiation delivered over the spine for spondylitis. Radiotherapy is an effective way to treat this rather disagreeable but not fatal disease. They have now studied about 14,000 of these patients. I have tried to compare the British and Japanese data but dissimilar populations make it extremely difficult. There were 9,000 to 11,000 heavily radiated people in the total Japanese population of Hiroshima (about 90,000). The Japanese received all their radiation in one day. The British patients received as much as 2500 roentgens but they received it in divided doses. In the Japanese there were 40 cases of leukemia, 31 in the heavily radiated, 9 in the less heavily radiated, whereas in a total of 21 cases in the British series 15 occurred in the more heavily radiated, 6 in the less heavily radiated.

There is some correlation of dosage in these groups as far as the degree of radiation is concerned. These two experiences, I think, do give some comparison. I should point out the strong implication from all these figures that everybody who is radiated is not going to get leukemia. Only 1 in 50 Japanese who were radiated severely enough to develop purpura, epilation and other severe radiation symptoms, developed leukemia. Radiation is certainly not the *sine qua non* of this condition. One must have the potential to develop leukemia in order to have radiation precipitate it; there are other factors, I am sure.

In reference to the British data, I am not at all sure that the large myeloid masses, such as the bone marrow of the spine and the pelvis in the adult, may not be end organs for leukemogenesis, and that there may not also be a strong analogy to the local radiation with relatively small amount of x-ray over the thymus in the small baby. The British, for example, have not proven that the fact that spondylitis is present may not well be a factor in the production of leukemia. This has been, as you know, one of the defects of this type of study. However, in the largest series I have seen reported the British have studied about 100 people with spondylitis who were not irradiated and none of them had leukemia. The British figures do indeed show statistically that there is ten times the incidence of leukemia in the irradiated group, but one must determine whether the patient wishes to go through life severely deformed or at least very uncomfortable, or whether he wants to take the one chance in 50 of developing leukemia some years hence.

I would like to point out that it takes a large dose of radiation to produce leukemia in man. This is true of one single dose. I am not so sure

that smaller doses given intermittently are not a good deal more carcinogenic and leukemogenic. I am also not happy about the possibility that some end organ or target organ might well be active. This might change considerably our ideas about radiation dosages and leukemogenesis.

Dr. Duffy:

The use of x-ray in childhood may involve an increased risk. There have been repeated reports of an association of x-radiation and increased incidence of thyroid cancer and leukemia in children. This association is not accepted by some radiologists (Clin. Proc. Child. Hosp., **11**: 209, 1955) but it is generally agreed that therapeutic x-ray should not be used in children unless absolutely necessary.

Obviously not all cancer in children is due to x-ray but there is a small, but highly significant, risk of the development of cancer in x-rayed children.

What might be the mechanism of this increased sensitivity? Besides the target-organ hypothesis mentioned by Dr. Moloney, there is an intriguing possibility that radiation is the *initiating* factor and the increased growth of the tissue (thyroid, bone marrow) in childhood is the *promoting* factor in the development of some types of juvenile cancer. This is a "two-way stretch" theory to cover the problem of age and x-ray cancer. It is suggested by the work of Stewart and Doniach and it is the subject of current investigation in our department.

Dr. Nelsen:

I might preface my remarks by saying that I attended the meeting of The National Committee for Radiation Protection and as a representative of the American Dental Association participated in the development of some of the handbooks published by this committee. Dentistry is statistically involved in this international problem of radiation, of course. Dr. Moloney's reference to 300 roentgens could refer to some of our old equipment, such as basket type, non-shielded tube, of which we must admit there are too many still in use.

I would like to read a few figures concerning the output of a properly filtered modern machine. The most common voltage used in dental radiology is approximately 55 kilovolts (kv). The amount of filter in the average dental machine is probably not as much as it could be. In the more modern dental machines and with a 6 second exposure, which is a long exposure, filtered with a millimeter and a half of aluminum, the patient is subjected to 1.2 roentgens per exposure. There is an average of 14 to 18 exposures per full mouth survey, and some simple arithmetic gives a lesser figure than 300 roentgens.

While we might possibly still have some situations where 300 roentgens is the total amount of exposure for a full mouth x-ray, these are exposures obtained by obsolete technique. Dental schools are trying their best, as are their medical counterparts, to make dental practitioners aware of the problems attached to the use of dental radiation. I think we are succeeding quite well.

In children, we are trying to reduce the routine use of x-rays to those which are absolutely justifiable. One problem in the very small youngster which has not been resolved as yet is the problem of the size of the patient. The geometry of exposure places the tube head in rather close proximity to the youngster in the lower jaw exposures. We may find that some additional shielding is necessary in our diagnostic procedures on these small youngsters.

Dr. Duffy:

This also applies to the pregnant female where some scatter is inevitable, but is to be avoided by shielding with a lead apron.

Question:

We have been given some figures about relative risk of exposure of x-ray in terms of the total body, and then it has been narrowed down to locales through which x-rays might be applied. The point has been made that this is a difficult thing to translate; 5000 roentgens to a limited area is not the same thing as 100 roentgens to the total body. Does this imply that there is no use in keeping track of accumulated x-ray exposure in an individual, or if there is some use, why and how should it be done?

Dr. Miller:

The American College of Radiology states that it is impossible to keep radiation diaries accurately on all people who get radiation for all purposes. However, if you examine hospital ward charts I am sure you will find someone who has received radiation out of all proportion to the need. In one particular instance I remember a premature infant who had had 7 fluoroscopies and 75 roentgens to the thymus in the first 4 months of life. The baby certainly did not need all the fluoroscopic examinations, and I think from a pediatric standpoint did not need the treatment of the thymus. She had then received 200–300 unnecessary roentgens to the chest and could have gone on receiving fluoroscopy except that we noted that 7 exposures had already taken place. A rough "diary" of radiation exposure levels might assist the clinician in curtailing non-essential fluoroscopic examinations.

Question:

Must the total number of roentgens given even to a localized area be added up in the cumulative sense? In other words, what is the difference between 100 roentgens given at one time or one roentgen each day for 100 days or 10 roentgens a year, each year for 10 years?

Dr. Brent:

One roentgen given to a portion of the body at one time, and one roentgen given to another portion of the body at another time, is not two roentgens. Roentgens given to different portions of the body cannot be added. The same is true of one roentgen given in 100 different places in the body. This is not 100 roentgens to the whole body but can be added only where the same tissue is getting overlapping doses.

As you remember, roentgen is not dose delivered from a machine, it is dose received. It is the amount of energy dissipated in the tissue, and the damage produced thereby. Total body fractionated irradiation (with respect to time) will not be the same as if the total dose were given at once. The field of recovery rates and irreparable damage is too broad to be discussed here except to say that certain aspects of radiation damage are reparable.

Question:

What effect will the multiple x-rays necessary for the proper placement of congenitally dislocated hips have on the infant male's gonads? What is the panel's opinion concerning the use of radiation for hemangiomas? Finally, what effect would the large doses of post-operative radiation of Wilm's tumor have on the child?

Dr. Miller:

Infertility is very difficult to measure in a human being because the number of ova and the number of sperm available is sufficient to provide families of average size despite a marked reduction in spermatogenesis or oogenesis. In a study performed in New York it was shown that irradiating mice *in utero* caused the males to be quite infertile when they grew to maturity. The females were not quite so seriously affected.

In the treatment of hemangiomas I can only say that if the hemangiomas will respond to no other treatment, radium would seem justified to me. The effects would only be local. Conceivably this could nonetheless give rise to late detrimental effects of radiation. If the hemangioma is on the face and the irradiation involves a toothbud, it is quite possible to have hypoplasia of the dental enamel when the tooth finally erupts.

There have been reported cases of Wilm's tumor in which doses of radia-

tion over 1500 roentgens involved a growing bone center such as the head of the femur or the spine; as a result of this (essential) radiation, shortening of the leg, or scoliosis occurred. A large study of this sort was done in Boston and some scoliosis was discovered.

Dr. Duffy:

On behalf of the Medical and Dental Schools, and the Medical Education for National Defense Program I wish to thank the participants for a lively discussion.

We can now, I hope, better advise our patient, exercise reasonable caution in ordering x-ray studies, and be generally aware of the difference, sometimes subtle, between the use and abuse of the x-ray.

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UMBILICAL HERNIA

Hyun-Wha Kim (Oh), M.D.*

Umbilical hernias result from muscular and fascial defects of the abdominal wall at the point where it has been pierced by the blood vessels of the umbilical cord. Umbilical hernia is generally classified into 3 types: 1) omphalocele (also called "funicular hernia of the umbilicus", "hernia into the umbilical cord", "umbilical eventration", "amniotic hernia", and "exomphalos"), 2) infantile umbilical hernia, and 3) adult umbilical hernia. Whereas some authorities do include omphalocele as a type of umbilical hernia, many consider it to be in a separate category.

The umbilical hernia commonly seen in children is the infantile umbilical

* Assistant Chief Resident.

hernia; this condition rarely presents a surgical emergency in childhood. Strangulation of umbilical hernia in the adult female is not infrequent. It is advisable that surgical repair of the umbilical hernias in female children be done in early life after there is no further natural tendency to decrease in the size of the hernia. Herniorrhaphy in childhood is a simple procedure and complications are rare under present anesthetic management.

OMPHALOCELE

Normally, from the sixth to the tenth week of fetal life the coelomic cavity has a forward extension into the base of the umbilical cord; this extension contains loops of intestine. At this stage, the abdominal viscera grow at a greater rate than does the peritoneal cavity itself. After the tenth week of intrauterine life, the abdomen enlarges at an accelerated pace and the organs withdraw into the abdominal cavity. If the viscera fail to return completely into the abdominal cavity due to a developmental defect in the midline, or if the cavity has not enlarged sufficiently to receive the viscera, an omphalocele occurs. Any degree of arrest in development may occur: from a cavity containing most of the abdominal contents to a small protrusion of peritoneum at the umbilical end of the cord. The size of an omphalocele varies. The average is 6.0 to 8.0 cm. in diameter. The omphalocele is a relatively rare congenital anomaly and is reported to occur about once in every 5,000 to 6,000 births. The omphalocele is present at birth and is covered by a translucent membrane consisting of fused peritoneum and amniotic membrane through which the abdominal contents are directly exposed to view. The skin of the abdomen usually stops at the base of the omphalocele. In the first 24 hours of life, the sac is moist, but later it tends to dry with exposure to air and is prone to rupture. Peritonitis, frequently terminating fatally, supervenes. During the first 12 or 18 hours of life these babies rarely show any evidence of pain or altered physiology from the visceral displacement and exposure to the lower temperature. It is also rare to find any respiratory difficulty.

Important anomalies associated with omphalocele include serious ones such as congenital heart disease and imperforate anus; in addition, there are many minor ones. Gross reported that fifty-nine per cent of his series had some other anomaly and twenty-eight per cent of the babies had associated malrotation of the intestine and colon which occasionally caused intestinal obstruction during the post-operative period of omphalocele repair. The series of twenty cases reported by Gross contained ten deaths and ten survivals. Gross pointed out that there are three factors which influence the prognosis: 1) the contents of the sac; the presence of the liver in the sac is a poor prognostic sign because it suggests that the small peritoneal cavity causes difficulty in reducing the omphalocele and closing

the abdominal wall. On the other hand, if the sac contains only small intestine, the prognosis is excellent; 2) the size of the omphalocele; in Gross' series if the sac was less than 8.0 cm. in diameter there was a seventy-five per cent chance of survival, but if the sac was greater than 8.0 cm. in diameter there was a fifteen per cent chance of survival; 3) the age of the individual at operation; delayed operation is apt to be followed by infections of the operative wound which may lead to subsequent fatal peritonitis.

Treatment of the omphalocele is immediate surgery. There are two types of operation; when the omphalocele is small, a one-stage operation is performed, whereas when the omphalocele is large and the peritoneal cavity is not ample enough to receive the viscera, a two-stage operation is preferred. The one-stage operation consists of replacement of the various viscera, excision of the sac and suitable closure of the abdominal wall. The two-stage operation is designed for managing more extensive defects. The essential feature of this procedure is leaving the omphalocele membrane intact, cutting free, and widely undermining the surrounding skin, and then bringing huge cutaneous flaps together to cover the bulging omphalocele sac. A secondary closure of muscles and fasciae should be done some months later when the abdominal cavity has grown sufficiently to accomodate the intestines. Post operative complications are related to inadequate space in the abdomen for the hernia contents. These complications are: 1) upward displacement of the diaphragm with resultant respiratory distress, cyanosis, and death, 2) pressure on the inferior vena cava which impedes the return of blood from the lower abdomen and legs so that death may follow from circulatory collapse, 3) pressure on the stomach and intestine causing partial or complete obstruction. These complications are fatal if they occur in twelve to thirty hours.

INFANTILE UMBILICAL HERNIA

The infantile umbilical hernia is the usual type of umbilical hernia seen in pediatric practice. It rarely presents a surgical emergency in childhood, but strangulation or incarceration have occurred, and have been reported very infrequently. Frankau has reported one typical case of strangulated umbilical hernia occurring in an infant who presented symptoms for one day, was operated on promptly and recovered. The infantile umbilical hernia is not present at birth. It makes its appearance either shortly after birth or in the first year or two of life, usually following an episode of increased intra-abdominal pressure which may be an hourly event attending crying, straining, and coughing (as in pertussis). When there is a weakness in the scar tissue which normally closes the umbilicus, a small round mass protrudes through the navel. The infantile umbilical hernia is covered

with forward projecting peritoneum, subcutaneous fat, and skin. The skin and peritoneum at the apex of the umbilical dimple are densely adherent to the linea alba at the umbilicus.

Concerning the etiology, some authorities think there is abnormality in the disposition of the aponeurotic fibers about the fetal umbilical defect, since the healing of the umbilicus is essentially the same in all infants with approximately the same amount of scar tissue incident to the healing process. On the other hand, there seems to some familial tendency in that several children in one family will have this type of hernia. From a racial standpoint, this hernia is much more commonly seen in the members of the negro race than in the white race. It is also more common in girls (2:1) possibly because of the less well developed abdominal musculature. A high incidence of infantile umbilical hernia is associated with congenital cretinism. An accurate incidence of infantile umbical hernia is not known because this hernia does not present a surgical emergency in childhood and the physician is frequently not consulted. The reported incidence of infantile umbilical hernia varies from one to ten per cent in white children and up to as high as eighty per cent in negro children.

Diagnosis of infantile umbilical hernia is not difficult. The enlargement of the hernia when the patient is in the erect position or coughing and its disappearance in the recumbent position (unless the contents are adherent) makes the diagnosis. In most cases, the complaint is umbilical protrusion which becomes larger and more tense due to increased intra-abdominal pressure such as crying, standing, straining, and other exercises. When the physician is consulted it is usually because of the disfiguration or parental worry. In cases of incarceration or strangulation the contents of the sac are composed of omentum, omentum and small intestine, or omentum and colon. Large hernial sacs may ulcerate from pressure due to a binder or truss intended to effect a cure. Clinical symptoms of incarceration include an irreducible mass in the hernial sac accompanied by distension of the abdomen, apparent pain, nausea, vomiting, fever and increased pulse rate, and leukocytosis.

About half of the infantile umbilical hernias will be spontaneously cured as the child grows older and when the rectus muscles constrict and finally obliterate the hernial orifice.

If the hernias are one cm. or less in size after the first year of life, and the fascial ring is less than 7 or 8 mm. in diameter, the hernias usually obliterate as the child grows. The hernias 1.5 to 4.0 cm. or more in diameter should be repaired, particularly if there has been recurrent discomfort or tendency to increase in size. Surgical repair as an elective procedure can be deferred if there is no strangulation or incarceration until the child is 2 to 3 years old when there is less natural tendency for the hernia to diminish in size. Some would rather wait until 4 years of age because of the adverse

psychological effect from hospitalization or mother-child separation. Proper surgical repair of the hernia is a radical herniorrhaphy; the principle of this procedure is to restore the normal navel depression. This however, is not possible when the hernia is too large. Semicircular cutaneous incisions just below the bulge, or vertical, straight, paramedian incisions to the right or to the left of the hernia are preferred from the cosmetic standpoint. Gross incises in the umbilical folds and reports an excellent cosmetic effect.

Indications for, and age of elective surgery for umbilical hernia vary according to the physician and the surgeon consulted. After herniorrhaphy the wound should be supported by a firm pad and strapped for six weeks after operation (Boling). The results of herniorrhaphy are, in general, good, but a small percentage of hernias recur. Gross observed more than fifteen hundred hernias at the Children's Hospital in Boston during the 25 year period from 1915 through 1939. Three-hundred and sixty of this total required operation, and of this number three recurred and one patient died of pneumonia post-operatively. In another series of four-hundred and thirty-nine cases of umbilical hernias which Gross operated on during the period from 1940 through 1951, there was one recurrence and no deaths.

ADULT UMBILICAL HERNIA

The adult umbilical hernia usually has a two-fold etiologie basis; there must be a congenital defect in the umbilical scar together with a superimposed element of increased intra-abdominal pressure from such conditions as pregnancy (the most common etiologic factor), intestinal obstruction, chronic cough, or ascites; all may cause umbilical hernia without an antecedent history of such a hernia. A normally healed umbilicus however, will not develop a hernia. Obesity is often associated with umbilical hernia and it is considered as a contributing factor.

The adult umbilical hernia is common in persons of middle age, and not uncommon in the obese multiparous woman in her early twenties. It is not infrequent that an asymptomatic umbilical hernia in the female becomes painful during pregnancy. Although the symptoms may disappear after delivery, they frequently recur with the next pregnancy. In adults small asymptomatic defects in the umbilicus without a sac and without a transmitted impulse are a fairly common finding; there is usually a pea-sized non-tender lump in the umbilical dimple. If such congenital defects in the umbilical scar present, increased intra-abdominal pressure from whatever cause gradually pushes more and more omentum into the defect, and eventually the omentum pulls the colon into the hernia. Omentum in the hernia sac, because of repeated trauma, shortly becomes adherent to the sac, leading to incarceration. Vague upper gastrointestinal symptoms due to traction on the omentum are common. As the hernia enlarges and loops of intestine enter the sac, partial intestinal obstruction with its associated

symptoms may appear. Strangulation of the contents of this hernia is very common because of rigidity of the aponeurotic ring.

McIver reported one-hundred and forty-seven cases of strangulated hernias (Massachusetts General Hospital 1918–1929 series). In this report eighteen cases were strangulated umbilical hernias and five of the eighteen died after surgery. Intestinal necrosis was present in each case. The incidence of strangulation of umbilical hernia in females was three times more frequent than in males in McIver's series. The hernia was particularly prone to strangulation from the age period of forty to sixty. The contents of the strangulated umbilical hernias in the fatal cases were as follows: small intestine, 3; transverse colon and small intestine, 1; and transverse colon, 1. Frankau reported one-hundred and fifty-three cases of strangulated umbilical hernias; twenty-three occurred in males and one-hundred and thirty in females; the ratio between female and male was therefore 6:1. Sixty-two patients died (female 50, male 12). The maximum incidence of strangulation occurred between the ages of 50 and 70 years. Small intestine or small intestine and omentum formed the contents of the sac more than six times as often as large intestine and omentum. The mortality rate for simple herniotomy was 28.8 per cent, whereas in cases requiring treatment other than simple release of the strangulation, the mortality rate was 76 per cent. Strangulation of umbilical hernia in adult life is not frequent but the mortality in this surgical emergency in adult life is high. Since in adult umbilical hernias pregnancy is the most common etiologic factor to increase intra-abdominal pressure and since pregnancy is a physiologic change occurring in nearly all married women, female children who have umbilical hernias which have failed to respond to adhesive tape strapping have good reason to have surgical repair of their umbilical hernia in their early life. This may prevent or minimize the hazard of strangulation or incarceration of the hernia during pregnancy in later life.

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ACUTE SINUSITIS IN CHILDHOOD

Carlos N. Vicens, M.D.*

Infection of the accessory nasal sinuses occurs far more frequently in children than one would ordinarily suspect. Some authors have stated that it ranks as one of the common diseases of childhood, and that no infant reaches the age of one year without a sinus infection. Others go still further and assume sinus involvement in practically all acute nasal infections[1]. At the Ear, Nose and Throat Clinic at the Children's Hospital in Melbourne, Australia, Cantor found that 67 out of 100 children had a sinus infection[2]. Schoenberg found that 154 nurslings out of 232 showed empyema of one or more nasal accessory sinuses on routine autopsy[2]. Many other roentgenologists and otolaryngologists have demonstrated sinus disease in nearly every case of infantile and childhood otitis media. Sinus infection may be a frequent primary focus for mastoiditis, bronchitis, bronchiectasis, and infectious asthma. In a 14 year study of recurring and chronic cough in childhood, Brown found that chronic bronchitis, asthma and bronchiectasis were dependent almost invariably on chronic sinusitis[2].

The paranasal sinuses are paired pneumatic cavities which communicate with the nasal fossae; they are situated in the paranasal bones: superior maxilla, ethmoid, frontal, and sphenoid. These sinuses are filled with air and are lined with a mucous membrane which is directly continuous with the nasal mucosa. The sinuses first become differentiated as outpouchings of the nasal fossae during the fourth fetal month. The ethmoid air cells and the sphenoid sinuses begin primarily as constrictions of the nasal fossae, while the maxillary and frontal sinuses originate as more or less direct extensions from the nose. All the sinuses differentiate by the local evagination of the nasal mucous membrane with concurrent resorption of the overlying bone[3].

The ethmoid and maxillary sinuses are present at birth and, therefore, are more commonly infected in children. The sphenoid sinus is developed by the age of 3 years, and the frontal sinuses after the age of 5 years. Infection usually begins in infancy or early childhood with the exception of infection of the maxillary sinuses secondary to infected teeth, and sinusitis due to trauma[4].

Sinusitis may be infectious or allergic. Infectious sinusitis is characterized by a swelling of the mucosa due to edema, congestion, and polymorphonuclear cellular infiltration, thus reducing the air space which may be partially or completely filled with catarrhal or purulent exudate. Such reactions in the sinuses occur commonly in infections of the upper respiratory passages, and may persist after the active infection and its clinical

* Formerly, Resident, Children's Hospital.

manifestations have disappeared. In long standing disease, a thickening of the mucosa takes place, and retention cysts or mucoceles may occur[5]. In allergic sinusitis the pathology is that of edema. The membranes are swollen and pale; later there is dilatation of the blood vessels and cellular infiltration if infection supervenes. A normal nasal discharge has a pH of 7.5. The nasal discharge in pure allergic rhinitis is usually alkaline, while in infectious rhinitis it is very definitely acid[4].

Sinusitis may occur following infection in the neighboring lymphoid tissue, such as adenoids, or be due to stasis of nasal discharge, foreign body in the nose, anomalies of the nose, polyposis (polyps in the nose or paranasal sinuses are composed of edematous tissue and indicate allergy,[4] the "common cold" syndrome (providing the environment for secondary infection), and systemic diseases such as diabetes, malnutrition, avitaminosis, and endocrine dyscrasias.

The local factors interfere with the drainage from the nose by mechanical obstruction. The nasal secretion, already loaded with organisms, becomes mucopurulent, and it is a very easy matter for the infection to spread to the sinuses. Infected teeth, a common etiologic factor in adults, are of no consequence as a source of infection in young children. Cold, damp, and changeable weather, with frequent upper respiratory infections, may be a factor. Swimming pools may be a source of infection. An improper method of blowing the nose or sneezing, especially when children have acute rhinitis may be a direct cause; both sides of the nose should not be held at the same time when the child sneezes or blows his nose[6].

The two most common symptoms of sinusitis are nasal discharge and nasal obstruction. These symptoms are so common in infants and children that we are prone to look upon them as negligible. The sinuses are frequently diseased, but because of the ease with which they usually drain, recovery takes place without the infection having been detected. Sneezing is at times a persistent symptom when sinusitis is present. Sneezing without an explanation should arouse suspicion of sinus infection[6]. Fullness in the head or pain and headache may be present, depending on the degree of occlusion of the orifices. Headache, so constant in adults is infrequent in children, but may be encountered. The involvement of the sphenoid sinuses may give sub-occipital headaches and pain behind the eyes; anterior ethmoidal infection may give pain around the temples and eyes; posterior ethmoidal infection produces pain which follows the distribution of the trigeminal nerve, primarily over the mastoid area[1].

Purulent secretions in the nose are very significant. Acute ethmoiditis in infants and children may produce periorbital cellulitis with edema of soft tissues, redness of the skin and exophthalmos. Temperature and toxicity vary with the infection. A chronic cough of a paroxysmal character,

and resembling whooping cough, may be present[5]. Enlarged cervical lymph nodes and gastrointestinal upsets may also be manifestations of infection in the sinuses.

In older children, as in adults, transillumination of the sinuses may be very helpful in establishing a diagnosis, especially if the sinusitis is unilateral. In infants the results are equivocal.

X-ray findings are inaccurate in infants and children due to the size of the cavities, and because the margins of healthy sinuses are often indistinct. Sinuses are normally cloudy and opaque due to the relatively redundant normal mucous membranes of early infancy. X-ray diagnosis is made on the basis of reduction of air content, and changes in the definition of the underlying bony margins. A thickening of the extra-sinus soft tissues may occur with cellulitis of the face, associated with ethmoid and maxillary sinusitis; superimposed on the para nasal air spaces this may cause haziness. Blurring of the sinuses may also occur with allergic edema or with the edema of nephrosis[4, 3].

In the early stages very little treatment is necessary and there is a marked tendency for spontaneous cure except in cases where drainage of sinuses is impaired[7]. Treatment consists of bed rest in a warm, moist atmosphere, good diet and hygiene, systemic (penicillin is usually effective), antibiotics, analgesic, sedative, and local measures. Prophylaxis is very important, and contributing factors should be eradicated; e.g., control of allergy, removal of growths, correction of nasal abnormalities and hygienic regimen which will lessen the tendency to nasal infections[7, 8].

Pain may be relieved by establishment of adequate drainage and by the use of external heat over the affected area. Analgesics and sedatives can be added if necessary. Local treatment is directed at obtaining adequate ventilation and drainage of sinuses and nasal cavities. It consists mainly of the instillation of carefully selected nose drugs, such as solutions of ephedrine, phenylephrine or naphazoline. Suction may be necessary at times to get adequate drainage and proper instillation of solutions. Suction and instillation may be done through either a suitable Asepto® syringe or the special suction instillation syringe of Proetz[7, 8]. Irrigation of the sinuses may be indicated when there is persistence of purulent exudate. The use of sprays and local nasal treatments has been said by some authors to be contraindicated because they interfere with ciliary action by thickening the mucous discharge, and may thus do more harm than good[4, 9]. The local nasal use of sulfonamides or antibiotics is not based on rational principles and their clinical value is negligible; they may in addition be irritating to the mucosa.

Surgery is very seldom required and should be avoided if possible. It is indicated when there is no relief of pain with conservative treatment, when

there is diseased bone, and when there are nasal defects or growths that interfere with drainage[7, 8].

Complications of acute sinusitis include otitis media, meningitis, cavernous sinus thrombosis, optic neuritis, orbital cellulitis and abscess, nephritis, septicemia, diarrhea, vomiting, bronchopneumonia, and chronic sinus infection. The prognosis of acute sinusitis is very good. Since the advent of antibiotics complications seldom occur and complete recovery is accomplished most of the time.

SUMMARY

Infection of the accessory nasal sinuses occurs more frequently in children than is suspected. Sinusitis may be a primary source for mastoiditis, bronchitis, bronchiectasis, infectious asthma, and other diseases. Infection of the maxillary and ethmoid sinuses is more common than that of the frontal and sphenoid sinuses, primarily because the first two are present at birth. Sinusitis may occur following an infection of the neighboring lymphoid tissues, or a common cold, or be due to foreign bodies in the nose, anomalies of the nose, polyposis, malnutrition, and a number of systemic diseases. X-ray diagnosis is very difficult, and transillumination is of little value in the younger group. The treatment consists of rest, good hygiene, antibiotics, shrinkage of the mucosa, and establishment of adequate drainage. Local antibiotics are of no value. The prognosis of acute sinusitis is very good, but if not adequately treated there may occur a very distressing and prolonged chronic sinusitis.

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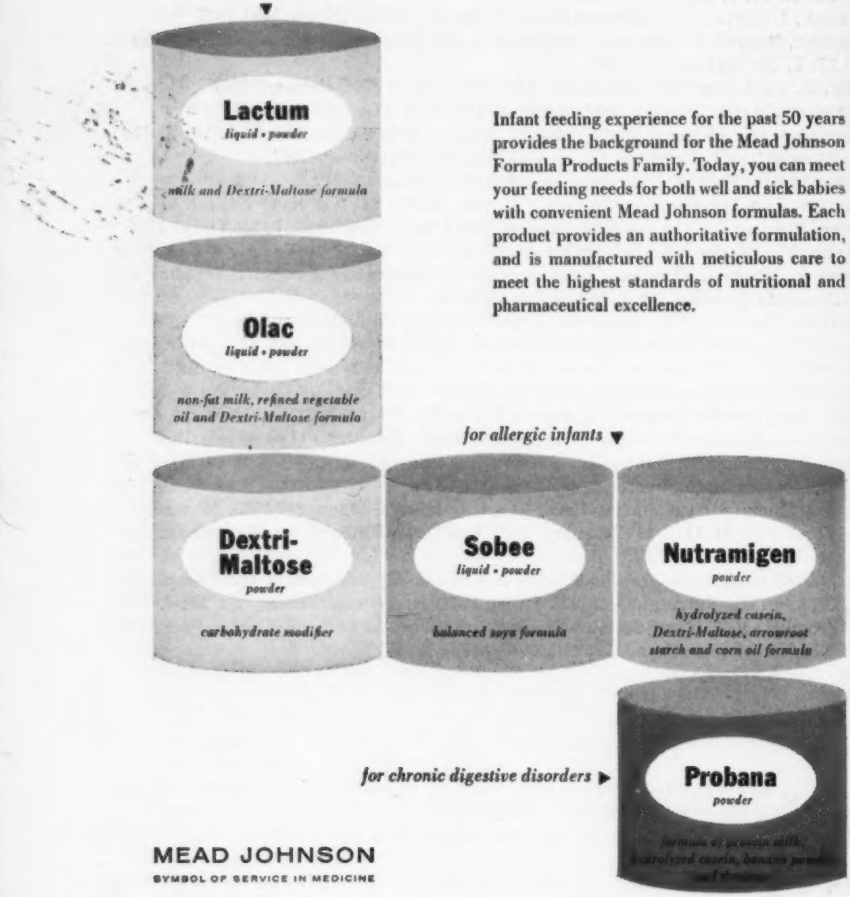

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